PATENT
4518-0107PUS1

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	LOIBNER, Hans et al.	Conf.:
Appl. No.:	NEW	Group:
Filed:	December 23, 2004	Examiner:
For:	USE OF A PREPARATION BASED ON ANANTIBODY DIRECTED AGAINST A TUMOR-ASSOCIATED GLYCOSYLATION	

L E T T E R

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

December 23, 2004

Sir:

The PTO is requested to use the amended sheets/claims attached hereto *(which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34))* during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment(s)

Claims:

1. The use of a preparation based on an antibody directed against a tumor-associated glycosylation for preparing a medicament for the prophylactic and/or therapeutic treatment for the reduction or inhibition, respectively, of the growth of tumor cells in a cancer patient by inhibiting glycosylated tumor cell receptors.

2. The use according to claim 1 for treating a patient in combination with a chemotherapy.

3. The use according to claim 1 for treating a chemotherapy-resistance.

4. The use according to claim 1 for treating the "minimal residual disease".

5. The use according to any one of claims 1 to 4 for preventing the mitogenic stimulation of a tumor cell by the epidermal growth factor (EGF) and/or by heregulin.

6. The use according to any one of claims 1 to 5 for the lysis of tumor cells which express a receptor from the family of the EGF receptors.

7. The use according to any one of claims 1 to 6, characterised in that an antibody is directed against Lewis antigens.

8. The use according to any one of claims 1 to 7, characterised in that an antibody directed against an aberrant glycosylation is used, like Lewis x-, Lewis b- and Lewis-y-structures, as well as sialyl-Tn, Tn antigen, GloboH, KH1, TF antigen and alpha-1,3-galactosyl epitope.

9. The use according to any one of claims 1 to 8, characterised in that the antibody is a monoclonal antibody, in particular a human, humanized, chimeric or murine antibody.

10. The use according to any one of claims 1 to 9, character-

ised in that an antibody having an affinity to binding the EGF receptor with a dissociation constant of below a Kd value of 10^{-6} mol/l, preferably less than 10^{-7}mol/l, most preferred 10^{-8}mol/l, or less, is used.

11. The use according to any one of claims 1 to 10, characterised in that the antibody is used in a dose of at least 50 mg, preferably at least 100 mg, most preferred at least 200 mg, up to 2 g per patient.

12. The use according to any one of claims 1 to 11, characterised in that an antibody derivative is used which comprises at least the Fab-portion of an antibody and binds to a tumor-associated glycosylation.

13. The use according to any one of claims 1 to 12, characterised in that the patient suffers from a cancer with tumor cells which express a receptor from the family of the EGF receptors.

14. A pharmaceutical preparation for treating cancer patients and containing an antibody directed against a tumor-associated glycosylation at a concentration ranging from 0.1-10%, preferably 1-5%.

15. A preparation for the pharmaceutical and/or diagnostic use, based on an antibody derivative comprising at least a Fab-portion of an antibody which binds to a tumor-associated glycosylation and has a CDC and ADCC activity of less than 50% of the native antibody.

16. The use according to any one of claims 1 to 13, characterised in that a body fluid or a tissue from a cancer patient is treated ex vivo, in particular bone marrow, blood, serum or organ components.

17. The use according to claim 16, characterised in that the cancer patient is treated within the frame of a high dosage chemotherapy.

18. The use according to claim 16, characterised in that the

body fluid, or the tissue, respectively, is derived from a patient with the risk of a cancer disease.

19. A method of producing a preparation based on a body fluid or tissue, in particular bone marrow, blood, serum or organ components, by

- ex vivo treatment of the body fluid or of the tissue with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex, and
- optionally separating the immune complex.

20. A preparation obtainable by a method according to claim 18 and having a reduced content of receptors from the EGF-receptor family.

21. A method of determining the risk of metastasis formation in a cancer patient, by

- providing a sample of a body fluid from a cancer patient,
- contacting said sample with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex of potentially present tumor cells with said antibody, and
- qualitative and/or quantitative determination of the immune complex in the body fluid as a measure of the metastasis-forming potential.

22. A diagnostic agent, containing an antibody directed against a tumor-associated glycosylation in combination with a carrier for separating a cellular immune complex.

23. A diagnostic agent containing an antibody directed against a tumor-associated glycosylation in combination with a labelling for determining a cellular immune complex.

Claims:

1. The use of a preparation based on an antibody directed against a tumor-associated glycosylation for preparing a medicament for the prophylactic and/or therapeutic treatment for the reduction or inhibition, respectively, of the growth of tumor cells in a cancer patient.

2. The use according to claim 1 for treating a patient in combination with a chemotherapy.

3. The used according to claim 1 for treating a chemotherapy-resistance.

4. The use according to claim 1 for treating the "minimal residual disease".

5. The use according to any one of claims 1 to 4 for inhibiting glycosylated tumor cell receptors.

6. The use according to claim 5 for preventing the mitogenic stimulation of a tumor cell by the epidermal growth factor (EGF) and/or by heregulin.

7. The use according to any one of claims 1 to 6 for the lysis of tumor cells which express a receptor from the family of the EGF receptors.

8. The use according to any one of claims 1 to 7, characterised in that an antibody is directed against Lewis antigens.

9. The use according to any one of claims 1 to 8, characterised in that an antibody directed against an aberrant glycosylation is used, like Lewis x-, Lewis b- and Lewis-y-structures, as well as sialyl-Tn, Tn antigen, GloboH, KH1, TF antigen and alpha-1,3-galactosyl epitope.

10. The use according to any one of claims 1 to 9, characterised in that the antibody is a monoclonal antibody, in particular a human, humanized, chimeric or murine antibody.

11. The use according to any one of claims 1 to 10, characterised in that an antibody having an affinity to binding the EGF receptor with a dissociation constant of below a Kd value of 10^{-6} mol/l, preferably less than 10^{-7}mol/l, most preferred 10^{-8}mol/l, or less, is used.

12. The use according to any one of claims 1 to 11, characterised in that the antibody is used in a dose of at least 50 mg, preferably at least 100 mg, most preferred at least 200 mg, up to 2 g per patient.

13. The use according to any one of claims 1 to 12, characterised in that an antibody derivative is used which comprises at least the Fab-portion of an antibody and binds to a tumor-associated glycosylation.

14. The use according to any one of claims 1 to 13, characterised in that the patient suffers from a cancer with tumor cells which express a receptor from the family of the EGF receptors.

15. A pharmaceutical preparation for treating cancer patients and containing an antibody directed against a tumor-associated glycosylation at a concentration ranging from 0.1-10%, preferably 1-5%.

16. A preparation for the pharmaceutical and/or diagnostic use, based on an antibody derivative comprising at least a Fab-portion of an antibody which binds to a tumor-associated glycosylation and has a CDC and ADCC activity of less than 50% of the native antibody.

17. The use according to any one of claims 1 to 14, characterised in that a body fluid or a tissue from a cancer patient is treated ex vivo, in particular bone marrow, blood, serum or organ components.

18. The use according to claim 17, characterised in that the cancer patient is treated within the frame of a high dosage chemotherapy.

19. The use according to claim 17, characterised in that the body fluid, or the tissue, respectively, is derived from a patient with the risk of a cancer disease.

20. A method of producing a preparation based on a body fluid or tissue, in particular bone marrow, blood, serum or organ components, by

- ex vivo treatment of the body fluid or of the tissue with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex, and
- optionally separating the immune complex.

21. A preparation obtainable by a method according to claim 19 and having a reduced content of receptors from the EGF-receptor family.

22. A method of determining the risk of metastasis formation in a cancer patient, by

- providing a sample of a body fluid from a cancer patient,
- contacting said sample with an antibody directed against a tumor-associated glycosylation for forming a cellular immune complex of potentially present tumor cells with said antibody, and
- qualitative and/or quantitative determination of the immune complex in the body fluid as a measure of the metastasis-forming potential.

23. A diagnostic agent, containing an antibody directed against a tumor-associated glycosylation in combination with a carrier for separating a cellular immune complex.

24. A diagnostic agent containing an antibody directed against a tumor-associated glycosylation in combination with a labelling for determining a cellular immune complex.